Association Between Sleep and Severe Periodontitis in a Nationally Representative Adult U.S. Population

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One-Sentence Summary: Adequate sleep may reduce severe periodontal disease, particularly in diabetic individuals.

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Author Contribution

Hend Alqaderi designed the study, contributed to data analysis, took the lead in writing the manuscript, and were in charge of overall direction and planning; J. Max Goodson contributed to data analysis, contributed to the interpretation of the results, and critically revised the manuscript; Israel Agaku contributed in the study design, carry out the statistical coding, and verified the analytical methods. All authors provided critical feedback and helped shape the research, analysis and manuscript, and gave final approval and agreed to be accountable for all aspects of the work.

ABSTRACT

Background: Poor sleep behavior appears to have adverse effects on health by metabolic disruption and immunity suppression. Sleep disturbance is strongly associated with diabetes, cardiovascular diseases, and some cancers. This study aimed to evaluate the association between sleep duration and periodontal disease in a national U.S. population study in a National Health and Nutrition Examination Survey (NHANES).

Methods: The data were collected from individuals aged ≥30 and older, and included 3,624 individuals in the United States, participants in NHANES 2013 to 2014.

A weighted multivariable logistic regression modeling quantified the association between sleep and severe periodontal disease. We tested for diabetes as an effect modifier, adjusting for potential confounders such as smoking status, sex, age, education level and dental visit.

Results: Individuals who sleep more than 7 hours/night with no trouble sleeping are 40% less likely to have severe periodontal disease (OR = 0.6, P<0.05), adjusting for age, sex, smoking status, FPL, education level, and dental visit. Additionally, diabetes was a significant positive effect modifier of the relation between sleep and severe periodontal disease (OR=4.8, P<0.05).

Conclusion: Findings of this cross-sectional representative study of an adult U.S. population revealed a statistically significant association between sleep duration and severe periodontitis. In this study, individuals who slept more than 7 hours/night were less likely to exhibit severe periodontal disease. It also seems that this relationship was stronger among diabetic individuals compared to non-diabetic individuals.

Keywords: Nutrition Survey, Periodontal Disease, Diabetes Mellitus, smoking, Oral Health, Public Health, United States.

INTRODUCTION

Insufficient sleep is a well-established risk factor that negatively affects daytime functioning and contributes to the progression of several chronic conditions [1] such as diabetes, cardiovascular, and other inflammatory disorders [2-4].

Recent studies show that healthy sleep behavior supports the immune system by regulating the defense mechanism against pathogens [5]. Additionally, sleep curtailment is associated with insulin resistance and glucose intolerance due to hormonal disruption [6]. Glucose intolerance is a causal risk factor for endothelial inflammation in both diabetic and non-diabetic individuals, compromising microvasculature and impairing wound healing [7]. A study of 30 sleep-deprived adults who slept at 3 a.m. to 7 a.m. found significantly higher levels of monocyte production of interleukin-6 and tumor necrosis factor alpha [8]. Another study on healthy subjects found that one night of sleep loss stimulates interleukin-1beta and interleukin-1 receptor antagonist [9]. It seems that short sleep duration has a potential systemic inflammatory effect that might subject endothelial tissue to bacterial infection.

We hypothesize that adequate sleep duration could be protective from severe periodontal disease as influenced by metabolic regulation and host immune response.

We also hypothesize that the effect of sleep duration could affect both diabetic and non-diabetic individuals differently, giving the fact that diabetes can intensify the association between sleep and severe periodontal disease. In addition, we examined whether smoking status is related to the association between sleep duration and periodontal disease.

A substantial body of evidence reports that adequate night sleep regulates insulin balance through circadian system processes [10] and that sleep deprivation is strongly related to glucose intolerance [7, 11].

There is an active link between sleep disorder, glucose intolerance, and systemic inflammation in non-diabetic patients [7, 11]. Periodontal destruction is associated with an inflammatory process of the supporting tooth structure, is a product of bacterial infection and immune host response [12]. Periodontal disease is characterized by gingival inflammation, periodontal pocket formation, loss of connective tissue attachment, and alveolar bone destruction, ultimately resulting in tooth loss [13, 14].

Evidence over the years shows that periodontal disease is strongly related to diabetes mellitus due to compromised microvasculature and inadequate host immune response [15]. Studies showed that the existing of cell-mediated immune responses in the periodontium is critical to causing damage to host tissue via immune or inflammatory interactions [16]. Both hormonal and cell-mediated immune responses play important roles in the host defense against microbial infectious disease such as periodontal diseases [17].

The purpose of this analysis was to investigate the cross-sectional association between sleep duration and severe periodontitis, mediated by diabetes. We used the National Health and Nutritional Examination Survey (NHANES, 2013 to 2014), to obtain a representative sample of the U.S population. The reason we used the 2013 – 2014 dataset is that this is the latest data that included a periodontal examination.

It is important to note that a study published by Wiener 18 used the NHANES dataset of 2011 – 2012 and failed to detect a significant relationship between sleep duration and periodontal disease [18]. Our study is different because we restricted our analysis to subjects with severe periodontitis, while the analysis of Weiner included subjects with any level of periodontal disease[18]. In addition, we aimed to determine the effect of diabetes on the relation between sleep duration and severe periodontitis.

METHODS

Study Population

This study used the public-use NHANES cross-sectional survey for years 2013 to 2014, in compliance with the Data Use Restrictions for data collected by the National Center for Health Statistics, Centers for Disease Control and Prevention [19]. The NHANES is a rich source of health/disease and risk factor data representative of the US population, obtained from a well-designed and well-conducted study starting from 1999. NHANES is a complex, multistage, stratified, clustered sample of the civilian, non-institutionalized US population, representing the US population. The NHANES includes a questionnaire, laboratory assays, and clinical examination measures of health outcomes and explanatory variables.

Nearly 5,000 participants of all ages were interviewed in their homes and received a health examination in Mobile Examination Centers. Dental surveys, including full-mouth periodontal examination involving participants' aged ≥30 years and above, were conducted by calibrated dental providers on the Mobile Examination Centers.

Details on NHANES methodology, the oral health exams and questionnaires, and related data quality assurance can be found elsewhere [19].

Description of the Dependent Variable

Periodontal examination:

The NHANES study of 2013-2014 was conducted using a full-mouth periodontal examination (FMPE) among individuals 30 years and older who did not have a health condition that required antibiotic prophylaxis before periodontal testing. The FMPE was conducted with the intent to produce gold-standard assessments for clinical attachment loss (CAL). For this reason, direct measurements of both the distance between the cementoenamel junction and the free gingival margin (CEJ-FGM) and the pocket depth (PD) were measured at each site. All measurements were taken at six sites (mesiobuccal, midbuccal distobuccal, mesiolingual, midlingual, and distolingual) of all teeth with the exclusion of third molars. All calculations were rounded to the lower whole millimeter. CAL was calculated based on these two measurements.

Definition of the dependent variable: Severe Periodontal Disease:

The outcome variable was defined as any individual with severe periodontal disease [20]. Severe periodontal disease was defined and coded as an individual having two or more

interproximal sites with ≥6 mm of loss of attachment not on the same tooth, and one or more interproximal sites with probing depths of ≥5 mm.

Description of independent and potentially confounding variables:

Sleep duration:

The primary exposure variable, sleep duration, was defined as a binary variable, and was coded using two sleep habit questions: 1) How much sleep do you usually get at night on weekdays or workdays? Also, 2) Have you ever told a doctor that you have trouble sleeping.

The recommended daily sleep hours for adults are 7 hours or more per night [21, 22]. If the subjects answered that they usually get more than 7 hours/night, and if the subjects responded that they never told their doctor of their difficulty in sleeping, they were placed in the category of 'sleep duration > 7 hours/night', otherwise, they would be placed in the category of 'sleep duration ≤ 7 hours/night'.

The potential confounding or effect modifier variables included are:

Diabetes:

This variable was binary. Each was asked; have you ever been told by a doctor or health professional that you have diabetes or sugar diabetes? The responses were one of the following: no, yes, or borderline. Each response was dichotomized to one of 2 categories: 'no' and either 'yes' or 'borderline'. Given the fact that 'borderline' might indicate a pre-diabetic status.

Smoking status:

From participants' responses to the smoking questions administered in the household interview, smoking status was defined as current, and never smokers [23]. Current smokers were defined as adults

who reported that they smoked 100 cigarettes or more in their lifetime, and they currently smoke every day or some days. Nonsmokers were defined as adults who reported that they have never smoked 100 cigarettes in their lifetime.

Age in years was categorized into four groups: 30 - 34 years, 35 – 49 years, 50 – 64, and 60 years and older. Sex was a binary variable as males and females. Education level variable was categorized as 0-11th grade, high school graduates or equivalent, and high school or above.

Race variable was categorized as Mexican-American, white, black, or other. We used the ratio of income to Federal Poverty Level (FPL) to indicate the financial status; this variable was categorized as < 100% FPL, 100%-199%FPL, 200%-399%FPL, and 400%+FPL. Dental visit variable includes four categories of the responses of the question: About how long has it been since you last visited a dentist? Include all types of dentists, such as orthodontists, oral surgeons, and all other dental specialists, as well as dental hygienists. The responses were one of the following: 6 months or less, more than 6 months but not more than 1 year ago, more than 1 year but not more than 2 years ago, more than 2 years ago or never.

Statistical Methods

We conducted multivariate binary logistic regression modeling to test the hypotheses that sleeping > 7 hours might be protective from severe periodontal disease, adjusting for smoking status, age, sex, dental visits, and education level. To determine the effect of diabetes on the relation between sleep and severe periodontal disease, we created an interaction term variable of the main effect of 'sleep' variable with 'diabetes' variable to

examine the effect of diabetes on the relation between sleep and periodontal disease. Similarly, we created an interaction term variable of 'sleep' variable with 'smoking' variable. We also compared the crude and the adjusted odds ratio of both diabetes and smoking status. By this comparison, we assess whether these factors are confounding factors in the relationship between severe periodontitis and sleep duration. Analyses were conducted using survey weights and to account for the sampling design to produce representative estimates for the United States. All analysis was performed using STAT 12 software, considering the significance level of 0.05.

RESULTS

Table 1 demonstrates the descriptive summary of the population characteristic comparing individuals with severe periodontal disease to individuals with no severe periodontal disease (p-values determined using the chi-square test). Among all the 3,624 individuals in the sample, 317 (8.7%) had severe periodontal disease. 73.2% of the individuals who exhibited severe periodontal disease reported short sleep duration (less than 7 hours) with a problem in sleeping. Ninety percent (90.2%) of those who did not demonstrate severe periodontal disease were not diabetic. Forty-nine percent of individuals classified with severe periodontitis were current smokers, whereas 52% of individuals classified as having no severe periodontitis were nonsmokers.

Males exhibited greater severity of periodontal disease (68.1%) compared to females (31.9%). Individuals' age 50 – 64 years old had the highest prevalence of severe periodontal disease (50.4%), compared to other age groups. Other demographic characteristics are presented in Table 1.

The present study (Table 2) indicates that individuals who slept more than 7 hours/night with no trouble sleeping are 40% less likely to have severe periodontal disease (OR = 0.6, P<0.05). Additionally, there is a significant positive effect of diabetes on the relation between sleep and severe periodontal disease (OR=4.8, P=0.01). i.e., diabetes is a significant effect modifier that intensifies the relationship between sleep and severe periodontal disease. There was no difference between the crude and the adjusted OR of being diabetic, indicating that diabetes is not a confounding factor in the relationship between severe periodontitis and sleep duration.

When testing for smoking effect, smoking status was not an effect modifier neither a confounding factor in the relation between periodontal diseases and sleep duration.

Individuals holding high school degree and above are less likely to exhibit severe periodontitis than other lower degrees (OR=0.2, P<0.001).

Older individuals were more likely to demonstrate periodontal disease than individuals' age 30 – 34 years old (OR=2.6, P=0.02), individuals age 50 -64 (OR=6.1, P<0.01) and individuals >60 (OR= 3.0, P=0.01).

Individuals living at extreme Federal Poverty Levels (FPL) also had significantly greater periodontal disease. Although those with an FPL of 100%-199% did not have significantly higher periodontal disease (OR=0.8, P=0.4), those with an FPL of 200-399% (OR=0.5, p=0.04) and 400% or greater (OR=0.2, P<0.01) both had significantly greater periodontal disease. Frequency of dental visits was not significantly related to periodontal disease.

DISCUSSION

In this study, we have shown that individuals who sleep more than 7 hours/night and who have never reported having trouble sleeping were less likely to exhibit severe periodontal disease (OR = 0.6, P<0,05). More importantly, when we tested diabetes as an

effect modifier on the relationship between sleep and severe periodontal disease, we found that diabetes modifies this association. The result of the assessment of effect modification by diabetes status shows that diabetic individuals who slept longer had decreased risk of developing severe periodontitis. The clinical motivation behind the evaluation of effect modification is to identify whether the impact of sleep duration is different in diabetic versus non-diabetic individuals, given the link between sleep, diabetes, and periodontal disease [7, 11, 15, 24]. By obtaining a signification positive odds ratio (OR=4.8, P=0.01) due to interaction between sleep and diabetes, we found that the likelihood of exhibiting severe periodontitis was five times higher among diabetic individuals than the likelihood expressed among the non-diabetic individuals. Findings of this study indicate that sleep duration could be related to periodontal disease through glucose intolerance, particularly in diabetic individuals, due to compromised immune response. Night sleep deprivation disrupts circadian rhythm, which ultimately results in significant delays of melatonin secretion [2]. The melatonin hormone is released by the pineal gland during night sleep and is responsible for regulating insulin secretion [2]. Insufficient night sleep reduces melatonin and insulin secretion, resulting in consequent insulin resistance and glucose intolerance [24]. This suggests that increased glucose levels could cause complications, especially in diabetic individuals. There is considerable evidence that diabetes is strongly related to periodontal disease [15], and that sleep disturbance is a causal risk factor for diabetes [25]. Insufficient night sleep influences insulin resistance and glucose intolerance, resulting in compromised microvasculature and endothelial damage [15, 24]. Inflammation is enhanced in patients with hyperglycemia indexed by the higher level of inflammatory mediators. Specifically,

the cytokine TNF-alpha has been demonstrated to play a major role in the process of periodontal destruction [26]. These mediators reduce the ability of the host cells to kill bacteria, which may explain the lower capacity of tissue healing and repair in patients with glucose intolerance [7] that might result in gingival inflammation and consequent periodontal diseases. Periodontitis is a multifactorial disease; dental plaque, oral hygiene habits, socioeconomic status, and the systemic/immune condition can influence the severity of periodontitis [27]. Periodontal disease is a treatable and reversible disease that shares common risk factors with systemic disease conditions [28]. Sleep can be one of the other risk factors of gingival inflammation triggered by glucose intolerance[29]. Evaluation of the risk factors for diabetes reveals that the risk of developing diabetes associated with sleep disturbances is comparable to that of conventional risk factors such as diet and physical activity, and should be considered a clinical guideline for type 2 diabetes screening [30]. Recent evidence suggests the role of diminished sleep in promoting inflammation and tissue damage through compromising immunity and disturbing glucose metabolism [5].

A study among healthy subjects showed that intentionally delaying night sleep and disturbing circadian rhythm resulted in hyperglycemia [31]. Moreover, considerable evidence indicates that insufficient sleep can trigger inflammation in different body organs due to hormonal disruption [32]. Experimental trials found that night sleep deprivation suppresses immunity, observed by increased cytokines inflammatory markers, with a dose-response relation [5]. Immune impairment by insufficient night's sleep is suggested by the poor antibody response to flu and hepatitis vaccines observed in subjects deprived of sleep [33, 34].

A recent longitudinal study has shown that children who slept fewer night hours, and children with higher glucose levels were more susceptible to develop gingival inflammation. This observation suggests that reduced sleep seems to be associated with gingival inflammation triggered by hyperglycemia [29].

The relationship between high blood glucose levels and increased gingivitis has been observed by others [11]. It follows that sleep disturbance can produce hyperglycemia that creates glucose intolerance, augmented gingival inflammation, and tissue damage that may precede periodontitis. Our present study supports these findings of the protective effect of healthy sleep habit on periodontal disease, mediated by the level of diabetes.

Several investigators have reported the relationship between sleep and periodontal disease. A study conducted in India with 60 subjects revealed a statistically significant relationship between the level of sleep deprivation and the severity of periodontal disease [35]. Another study of 99 subjects conducted in Turkey showed that the grade of periodontitis was associated with short sleep duration and low sleep quality [36]. On the other hand, three cross-sectional studies were published using the Korean NHANES (KNHANES) 2012, failed to detect a relationship between short sleep duration and periodontal disease, instead these three studies reported that long sleep duration was associated with periodontal disease [18, 37, 38]. It is worth mentioning that these three KNHANES studies used different measurements of periodontitis. The presence of periodontitis in the KNHANES was defined as at least two interproximal sites with an attachment loss of at least 3mm and at least two interproximal sites with probing depths of at least 4mm, which are not on the same tooth or at least one site with

a probing depth of at least 5 mm. In our study, we restricted the analysis to only severe periodontal disease.

Additionally, a meta-analysis published in 2015 showed some evidence of the association, but not a causal effect, between periodontal disease and Obstructive Sleep Apnea (OSA) [39]. In addition to the studies included in the meta-analysis, and regardless of the variation in measuring periodontitis and OSA, recent studies reported consistent results that OSA is associated with periodontal disease [40, 41]. Because both conditions are related to systemic inflammation, it is plausible that OSA influences the activation of inflammatory pathways in periodontal inflammation or vice versa [40]. Sleep behavior has a critical influence on metabolic health and immunity [42]. There is a strong link between periodontal disease with immune reaction and metabolic regulation.

Smoking, sleep, and periodontal disease

In this analysis, we failed to detect a significant effect of smoking status on the relationship between severe periodontal disease and sleep duration. Lack of sleep quality data might contribute to this finding. Most of the published studies on the relationship between smoking and sleep used sleep quality data along with the sleep quantity data. A study among 6,400 participants of the Sleep Heart Health Study (the United States, 1994–1999) found no differences in sleep architecture between former and never smokers; however, they suggested that acute withdrawal from nicotine in cigarette smoke may contribute to disturbances in sleep architecture [43]. Compared to nonsmokers, Jaehne et al., 2012 reported that smokers showed insomnia-like sleep impairments, but no differences in sleep disorder parameters as well as in the sleep efficiency measured by Polysomnography between smokers and nonsmokers [44]. A cohort of 10th graders in the US shows that the associations between

smoking and sleep problems exist, but these associations were different between non-Hispanic Black and non-Hispanic White youth, and they recommend that sleep problems intervention studies should include smoking as a secondary outcome to better understand how intervening on one behavior could influence other behavior [45]. There is emerging evidence though shows that poor sleep quality is associated with smoking status [46, 47]. A study of adults aged 20 years and above from the 2005–2006 National Health and Nutrition Examination Survey, found that current smokers reported significantly more sleep difficulties than non-smokers [23]. Similarly, a study among Chinese adolescents found that adolescents with poor sleep quality were more likely to smoke [47].

On the other hand, the evidence on the relationship between smoking and periodontal disease is clear and well-established. Cigarette smoking increases the incidence, severity, and progression of periodontal diseases [37, 48], indexed by the nicotine and chemicals effect that diminish the attachment and augmentation of gingival fibroblasts and periodontal ligament cells [49, 50].

In conclusion, this study suggests a protective effect of healthy sleep hours (>7h/night) on severe periodontal disease, and this relation is stronger among diabetic individuals. It appears that diabetic individuals benefit more from the protective effect of healthy sleep on periodontal disease.

These understandings may help in the development of new preventive and therapeutic approaches against periodontal disease by enhancing the quality of sleep behavior. However, further prospective longitudinal studies are needed for better assessment of the protective effect of sleep behavior on periodontal disease.

Study Limitations

The self-reported questions might be susceptible to reporting bias. The cross-sectional design of the current study allows only measuring the association but not the causation between sleep duration and severe periodontal disease. Moreover, the relation between sleep duration and periodontal disease could be influenced by other factors such as medical conditions, body weight, and certain hormones. Finally, the findings of this study apply only the adult U.S. population in 2014. Future studies should consider collecting data on sleep quality and not only sleep quantity to understand the effect of sleep on oral health better. Future studies should also consider prospective intervention and longitudinal data collection to infer the causal relation of sleep quantity and quality on periodontal health, using objective, unbiased measures and accounting for smoking and other possible confounding factors.

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REFERENCES

1. Moore M, Meltzer LJ, Mindell JA. Bedtime problems and night wakings in children. *Prim Care* 2008;35:569-581, viii.
2. Srinivasan V, Ohta Y, Espino J, et al. Metabolic syndrome, its pathophysiology and the role of melatonin. *Recent patents on endocrine, metabolic & immune drug discovery* 2013;7:11-25.
3. Knutson KL. Does inadequate sleep play a role in vulnerability to obesity? *American journal of human biology : the official journal of the Human Biology Council* 2012;24:361-371.
4. Narang I, Manlhiot C, Davies-Shaw J, et al. Sleep disturbance and cardiovascular risk in adolescents. *CMAJ : Canadian Medical Association journal = journal de l'Association medicale canadienne* 2012;184:E913-920.
5. Irwin MR. Why sleep is important for health: a psychoneuroimmunology perspective. *Annu Rev Psychol* 2015;66:143-172.
6. Dashti HS, Follis JL, Smith CE, et al. Habitual sleep duration is associated with BMI and macronutrient intake and may be modified by CLOCK genetic variants. *The American journal of clinical nutrition* 2014;101:135-143.
7. Berezin AE, Kremzer AA. Relationship between circulating endothelial progenitor cells and insulin resistance in non-diabetic patients with ischemic chronic heart failure. *Diabetes Metab Syndr* 2014;8:138-144.
8. Irwin MR, Wang M, Campomayor CO, Collado-Hidalgo A, Cole S. Sleep deprivation and activation of morning levels of cellular and genomic markers of inflammation. *Arch Intern Med* 2006;166:1756-1762.
9. Frey DJ, Fleshner M, Wright Jr KP. The effects of 40 hours of total sleep deprivation on inflammatory markers in healthy young adults. *Brain Behav Immun* 2007;21:1050-1057.
10. Gumenyuk V, Roth T, Drake CL. Circadian phase, sleepiness, and light exposure assessment in night workers with and without shift work disorder. *Chronobiology international* 2012;29:928-936.
11. Desouza CV, Hamel FG, Bidasee K, O'Connell K. Role of inflammation and insulin resistance in endothelial progenitor cell dysfunction. *Diabetes* 2011;60:1286-1294.
12. Darveau RP. Periodontitis: a polymicrobial disruption of host homeostasis. *Nat Rev Microbiol* 2010;8:481-490.

13. Socransky SS, Haffajee AD. Periodontal microbial ecology. *Periodontol 2000* 2005;38:135-187.

14. Paster BJ, Boches SK, Galvin JL, et al. Bacterial diversity in human subgingival plaque. *J Bacteriol* 2001;183:3770-3783.

15. Stanko P, Izakovicova Holla L. Bidirectional association between diabetes mellitus and inflammatory periodontal disease. A review. *Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub* 2014;158:35-38.

16. Teng Y-TA. The Role of Acquired Immunity and Periodontal Disease Progression. *Crit Rev Oral Biol Med* 2003;14:237-252.

17. Ebersole JL, Taubman MA. The protective nature of host responses in periodontal diseases. *Periodontol 2000* 1994;5:112-141.

18. Wiener RC. Relationship of routine inadequate sleep duration and periodontitis in a nationally representative sample. *Sleep disorders* 2016;2016.

19. . NCHS. National Health and Nutrition Examination Survey. Available at: http://www.cdc.gov/nchs/nhanes.htm.

20. Beltran-Aguilar ED, Eke PI, Thornton-Evans G, Petersen PE. Recording and surveillance systems for periodontal diseases. *Periodontol 2000* 2012;60:40-53.

21. Paruthi S, Brooks LJ, D'Ambrosio C, et al. Consensus statement of the American Academy of Sleep Medicine on the recommended amount of sleep for healthy children: methodology and discussion. *J Clin Sleep Med* 2016;12:1549-1561.

22. Badr MS, Belenky G, Bliwise DL, et al. Recommended amount of sleep for a healthy adult: a joint consensus statement of the American Academy of Sleep Medicine and Sleep Research Society. *J Clin Sleep Med* 2015;11:591-592.

23. McNamara JP, Wang J, Holiday DB, et al. Sleep disturbances associated with cigarette smoking. *Psychology, health & medicine* 2014;19:410-419.

24. Kim C-R, Song Y-M, Shin J-Y, Gim W. Association between sleep duration and impaired fasting glucose in korean adults: results from the korean national health and nutrition examination survey 2011–2012. *Korean journal of family medicine* 2016;37:51.

25. Lee SWH, Ng KY, Chin WK. The impact of sleep amount and sleep quality on glycemic control in type 2 diabetes: A systematic review and meta-analysis. *Sleep Med Rev* 2017;31:91-101.

26. Gurenlian JR. Inflammation: the relationship between oral health and systemic disease. *Dent Assist* 2009;78:8-10, 12-14, 38-40; quiz 41-13.

27. Trombelli L, Farina R. A review of factors influencing the incidence and severity of plaque-induced gingivitis. *Minerva stomatologica* 2013;62:207-234.

28. Papapanou PN. Systemic effects of periodontitis: lessons learned from research on atherosclerotic vascular disease and adverse pregnancy outcomes. *Int Dent J* 2015;65:283-291.

29. Alqaderi H, Tavares M, Hartman M, Goodson J. Effect of sleep and salivary glucose on gingivitis in children. *J Dent Res* 2016;95:1387-1393.

30. Anothaisintawee T, Reutrakul S, Van Cauter E, Thakkinstian A. Sleep disturbances compared to traditional risk factors for diabetes development: Systematic review and meta-analysis. *Sleep Med Rev* 2016;30:11-24.

31. Reutrakul S, Siwasaranond N, Nimitphong H, et al. Relationships among sleep timing, sleep duration and glycemic control in Type 2 diabetes in Thailand. *Chronobiol Int* 2015;32:1469-1476.

32. Li X, Tse HF, Jin LJ. Novel endothelial biomarkers: implications for periodontal disease and CVD. *J Dent Res* 2011;90:1062-1069.

33. Prather AA, Hall M, Fury JM, et al. Sleep and antibody response to hepatitis B vaccination. *Sleep* 2012;35:1063-1069.

34. Spiegel K, Sheridan JF, Van Cauter E. Effect of sleep deprivation on response to immunizaton. *Jama* 2002;288:1471-1472.

35. Grover V, Malhotra R, Kaur H. Exploring association between sleep deprivation and chronic periodontitis: A pilot study. *J Indian Soc Periodontol* 2015;19:304.

36. Karaaslan F, Dikilitaş A. The Association Between Stage‐Grade Of Periodontitis And Sleep Quality And Oral Health‐Related Quality Of Life. *J Periodontol* 2019.

37. Romandini M, Gioco G, Perfetti G, Deli G, Staderini E, Laforì A. The association between periodontitis and sleep duration. *Journal of clinical periodontology* 2017;44:490-501.

38. Han K, Park Y-M, Park J-B. Evaluation of an association between long sleep duration and periodontal disease among men and women using nationally representative data. *Gac Sanit* 2018;32:143-150.

39. Al-Jewair TS, Al-Jasser R, Almas K. Periodontitis and obstructive sleep apnea's bidirectional relationship: a systematic review and meta-analysis. *Sleep and Breathing* 2015;19:1111-1120.

40. Sanders AE, Essick GK, Beck JD, et al. Periodontitis and Sleep Disordered Breathing in the Hispanic Community Health Study/Study of Latinos. *Sleep* 2015;38:1195-1203.

41. Gamsiz‐Isik H, Kiyan E, Bingol Z, Baser U, Ademoglu E, Yalcin F. Does Obstructive Sleep Apnea Increase the Risk for Periodontal Disease? A Case‐Control Study. *Journal of periodontology* 2017;88:443-449.

42. Nedeltcheva AV, Scheer FA. Metabolic effects of sleep disruption, links to obesity and diabetes. *Curr Opin Endocrinol Diabetes Obes* 2014;21:293-298.

43. Zhang L, Samet J, Caffo B, Punjabi NM. Cigarette smoking and nocturnal sleep architecture. *American Journal of Epidemiology* 2006;164:529-537.

44. Jaehne A, Unbehaun T, Feige B, Lutz UC, Batra A, Riemann D. How smoking affects sleep: a polysomnographical analysis. *Sleep medicine* 2012;13:1286-1292.

45. Bellatorre A, Choi K, Lewin D, Haynie D, Simons-Morton B. Relationships between smoking and sleep problems in black and white adolescents. *Sleep* 2017;40.

46. Sabanayagam C, Shankar A. The association between active smoking, smokeless tobacco, second-hand smoke exposure and insufficient sleep. *Sleep medicine* 2011;12:7-11.

47. Chen H, Bo QG, Jia CX, Liu X. Sleep Problems in Relation to Smoking and Alcohol Use in Chinese Adolescents. *The Journal of nervous and mental disease* 2017;205:353-360.

48. Shin J, Lee S-W. The effect of cigarette smoking on Porphyromonas gingivalis, a crucial periodontal pathogen. *Oral Biology Research* 2019;43:17-22.

49. Giannopoulou C, Geinoz A, Cimasoni G. Effects of nicotine on periodontal ligament fibroblasts in vitro. *Journal of clinical periodontology* 1999;26:49-55.

50. Kubota M, Yanagita M, Mori K, et al. The effects of cigarette smoke condensate and nicotine on periodontal tissue in a periodontitis model mouse. *PloS one* 2016;11:e0155594.

Table 1. Descriptive Summary of the population characteristics with and without severe periodontal disease. Sleep duration=sleep >7h/night with no problem with sleeping, or otherwise. FPL=Federal Poverty Level. Current smokers= smoked 100 cigarettes and they currently smoke every day or somedays.

Group	Independent variable	Severe active periodontal disease (N=317)		No severe active periodontal disease (N=3,307)		Total (N=3,624)	P value
Sleep duration	> 7 hours/night	85	26.8%	1,013	30.6%	1,098(30.3%)	0.1
	≤ 7 hours/night	232	73.2%	2,294	69.4%	2,526(69.7%)	
	Diabetic or borderline	35	11%	325	9.8%	360 (9.9%)	
Smoking status	Current smokers	58	49%	572	47.3%	630(47.4%)	0.6
	Nonsmokers	60	51%	638	52.7%	698(52.6%)	
Age	Age 30 -34	13	4.1%	440	13.3%	453(12.50)	<0.001
	Age 35 - 49	71	22.4%	1,186	35.9%	1,257(34.69)	
	Age 50 -64	160	50.4%	963	29%	1,123(30.99)	
	Age > 60	73	23.1%	718	21.7%	791(21.83)	
Sex	Males	216	68.1%	1,539	46.5%	1,755(48.43)	<0.001
	Females	101	31.9%	1,768	53.5%	1,869 (51.57)	
Race	Mexican-American	86	27.1%	727	22%	813(22.4%)	<0.001
	White	s93	29.3%	1,472	44.5%	1,565(43.2)	
	Black	105	33.1%	602	18.2%	707(19.5%)	
	Other	33	10.4%	506	15.3%	539(14.87)	
Federal Poverty	< 100% FPL	95	33.3%	543	17.7%	638 (19.1%)	<0.001
	100%-	81	28.4%	735	24%	816 (24.4%)	

Level	199%FPL						
	200%-399%FPL	75	26.3%	833	27%	908 (27.1%)	
	400%+FPL	34	11.9%	951	31.1%	985 (29.4%)	
Dental Visit Frequency. Last dental visit is:	6 months or less	161	50.7%	1,577	47.7%	1,738 (48%)	0.6
	> than 6 months, but not >than 1 year ago	47	14.8%	481	14.5%	528 (14.6%)	
	> than 1 year, but not >than 2 years ago	32	10.1%	326	9.9%	358 (10%)	
	Last dental visit: more than 2 years, or never	77	24.3%	917	27.8%	994 (27.4%)	
Education level	0-11th grade	116	36.5%	599	18%	715 (19.7%)	<0.001
	High school graduate/GED	97	30.6%	689	21%	786 (21.7%)	
	High school or above	104	33%	2,017	61%	2,121 (58.5%)	

Table 2. Multiple logistic regression model for the association between severe periodontal disease with sleep duration: The United States, 2013 – 2014. *: P-Value <0.05. #: the interaction variable between sleep duration and diabetic status.

Independent variables	Adjusted Odds Ratio (P Value)	95% Confidence Interval
Sleep duration	0.6 (0.008) *	0.3-1.3
Diabetes	0.9 (0.8)	0.5-1.8
Sleep # diabetes (interaction term)	4.8 (0.01)*	1.4-15.8
Smoking status (Reference: nonsmoker)	0.1 (0.8)	0.5-1.9
Sex (Reference: male)	0.4 (<0.001)*	0.2-0.6
Age (Reference: age 30-34)		
Age 35 - 49	2.6 (0.02)*	1.2-5.7
Age 50 - 64	6.1 (0.001) *	2.5-14.8
Age > 60	3.0 (0.01)*	1.2-7.3
Education level (Reference: 0 -11th grade)		
High school graduate or equivalent	0.7 (0.3)	0.4-1.3
High school or above	0.2 (<0.001) *	0.1-0.4
Last dental visit (reference: 6 months or less)		
More than 6 months, but not more than 1 year ago	0.8 (0.5)	0.5-1.4
More than 1 year, but not more than 2 years ago	0.9 (0.8)	0.5-1.6
More than 2 years, or never	0.8 (0.4)	0.5-1.3
FPL (Reference: < 100% FPL)		
100%-199%FPL	0.8 (0.4)	0.6-1.2
200%-399%FPL	0.5 (0.04) *	0.3-0.9
400%FPL	0.2 (0.002) *	0.1-0.5